of which is modulated by PDX. The method includes measuring the expression of one or more nucleic acids in a test cell population exposed to a compound that modulates PDX activity or expression. Expression of the nucleic acid sequences in the test cell population is then compared to the expression of the nucleic acid sequences in a reference cell population, which is a cell population that has not been exposed to the compound, or, in some embodiments, a cell population exposed the compound. Comparison can be performed on test and reference samples measured concurrently or at temporally distinct times. An example of the latter is the use of compiled expression information, *e.g.*, a sequence database, which assembles information about expression levels of known sequences following administration of various agents. For example, alteration of expression levels following administration of compound can be compared to the expression changes observed in the nucleic acid sequences following administration of a control agent, such a PDX nucleic acid.

C3 Cancel

On page 28, please replace the paragraph beginning on line 16 with the following rewritten paragraph.

Animals were treated with recombinant adenovirus as described in EXAMPLE 2. Prohormone convertase 1/3 (PC1/3) gene expression was determined by RT-PCR as described in EXAMPLE 2 with the exception that cDNA was reverse-transcribed using a gene specific oligonucleotide (TCCAGGTGCCTACAG GATTCTCT) (SEQ ID NO: 1) instead of oligo $(dT)_{15}$). As demonstrated in FIG. 3 only livers from animals treated with PDX-1 exhibited the induction of PC1/3 expression, a member of the Kexin family proteases, PC1/3 expression is restricted to endocrine and neuroendocrine cells with regulated secretory pathway. Taken together with the capacity to retain the produced hormones in intracellular compartments suggests a PDX-1 dependent induction of an endocrine phenotype which includes the induction of a regulated pathway for hormone production, processing, storage and secretion.

C4

On page 29, please replace Table 1 with the following rewritten table.

**Table 1: RT-PCR analysis for determination of PDX-1 induced gene-expression.**

| Gene | Primer Sequences 5` - 3` | PCR Conditions | | | | | |
|---|---|---|---|---|---|---|---|
| | | PCR Product | Annealing | | Extention | | Cycles |
| | | | °C | sec | °C | sec | |
| Rat PDX-1 (ectopic) | F: CCAGTTTGCAGGCTCGCTGG (SEQ ID NO: 2)<br>R: GCTGCGTATGCACCTCCTGC (SEQ ID NO: 3) | 279 bp | 62 | 60 | 72 | 60 | 31 |
| Human Insulin (ectopic) | F:CTTTGTGAACCAACACCTGTGC (SEQ ID NO: 4)<br>R:GCAGATGCTGGTACAGCATTGT (SEQ ID NO: 5) | 239 bp | 63 | 60 | 72 | 60 | 38 |
| Mouse Insulin I | F: TTGCCCTCTGGGAGCCCAAA (SEQ ID NO: 6)<br>R: CAGATGCTGGTGCAGCACTG (SEQ ID NO: 7) | 253 bp | 62 | 60 | 72 | 60 | 38 |
| Mouse Insulin II | F: TCTTCCTCTGGGAGTCCCAC (SEQ ID NO: 8)<br>R: CAGATGCTGGTGCAGCACTG (SEQ ID NO: 9) | 259 bp | 62 | 60 | 72 | 60 | 38 |
| Mouse -actin | F: ATGGATGACGATATCGCT (SEQ ID NO: 10)<br>R: ATGAGGTAGTCTGTCAGGT (SEQ ID NO: 11) | 500 bp | 56 | 45 | 72 | 60 | 35 |
| Mouse PC1/3 | F: CTGGTTGTCTGGACCTCTGAGTA (SEQ ID NO: 12)<br>R: CCAACAGCAGAA GTGAGTGTGAC (SEQ ID NO: 13) | 361 bp | 55 | 45 | 72 | 60 | 38 |
| Mouse PDX-1 (endogenous) | F:CAAGCTCGCTGGGATCACTGGAGCAG (SEQ ID NO: 14)<br>R:GATGTGTCTCTCGGTCAAGTTCAACAT C (SEQ ID NO: 15) | 421 bp | 58 | 45 | 72 | 60 | 38 |
| Mouse & Rat somatostatin | F:CCTGGCTTTGGGCGGTGTCA (SEQ ID NO: 16)<br>R:CTCGGGCTCCAGGGCATCATTC (SEQ ID NO: 17) | 165 bp | 68 | 45 | 72 | 60 | 38 |
| Mouse glucagon | F:ACCAGCGACTACAGCAAATACCTC (SEQ ID NO: 18)<br>R:AGCAATGGCGACTTCTTCTGG (SEQ ID NO: 19) | 242 bp | 60 | 45 | 72 | 60 | 38 |
| rat insulin-1 | F:GTGACCAGCTACAATCATAG (SEQ ID NO: 20)<br>R:AGTTCTCCAGTTGGTAGAGG (SEQ ID NO: 21) | 370 bp | 57 | 45 | 72 | 60 | 38 |
| Rat -actin | F: CGTAAAGACCTCTATGCCAA (SEQ ID NO: 22)<br>R: AGCCATGCCAAATGTGTCAT (SEQ ID NO: 23) | 350 bp | 57 | 45 | 72 | 60 | 35 |

On page 35, please replace the paragraph beginning on line 26 with the following rewritten paragraph.

c6 **Example 14: IDENTIFICATION OF NUCLEIC ACIDS THE EXPRESSION OF WHICH IS MODULATED BY PDX**

On pages 35-36, please replace the paragraph beginning on line 27 with the following rewritten paragraph.

c7 Nucleic acids modulated by PDX are identified by ectopic PDX expression. Nucleic acids that are not expressed in control treated extra-pancreatic islet tissue, as compared to pancreatic tissue are the nucleic acids modulated by PDX. These nucleic acids so identified are used as therapeutic compounds to treat pancreatic associated disorders.

On page 36, please replace the paragraph beginning on line 2 with the following rewritten paragraph.

c8 Identification of the target genes is performed by either subtractive libraries, commercially available microarray Chips (Incyte, or Affimetrix), or membrane hybridizations (CLONTECH. Atlas™ expression arrays, or Multiple Tissue Northern (MTN®) Blots). RNA isolation from treated tissues, its purification, and cDNA probe synthesis is performed according to manufacturer instructions.

On page 37, please replace the paragraph beginning on line 10 with the following rewritten paragraph.

An additional method to analyze the activity of transcription factors is performed by footprinting, and by

c9 **Electro-Mobility Shift Assays (EMSA):** Nuclear extracts (3-4 μg of protein) were incubated on ice for 10 minutes in DNA binding mixture containing 10% Glycerol, 15 mM Hepes (pH 7.9), 150 mM KCl, 5 mM DTT and 0.3 μg of poly dIdC, poly dAdT (SIGMA St-Louis MO). After the first incubation, approximately 0.2 ng of the probe was added for an additional 25 minutes incubation on ice. The binding reaction was analyzed on a native 4% polyacrylamide gel.

On page 37, please replace the paragraph beginning on line 18 with the following